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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/962,094	10/31/1997	PATRICIA A. BILLING-MEDEL	5995.US.P1	8450

23492 7590 01/24/2003

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EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	38

DATE MAILED: 01/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/962,094	Applicant(s) Billing-Medel
	Examiner Jehanne Souaya	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 13, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-29, 31, 32, 34, 36, 37, 60-68, and 70-79* is/are pending in the application.

4a) Of the above, claim(s) *17-29, 31, 32, 34, 36, and 37* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *60-68 and 70-79* is/are rejected.

7) ☒ Claim(s) *66* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Souaya.

2. Currently, claims 17-29, 31, 32, 34, 36, 37, 60-68, and 70-79 are pending in the instant application. Claims 17-29, 31, 32, 34, 36, and 37 have been withdrawn from consideration as being drawn to non elected inventions. This office action is in response to the amendment filed 11/13/2002. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following office action contains new grounds of rejection and objection. The rejections herein applied constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is NON-FINAL.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 101

4. Claims 60-68 and 70-79 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility as set forth in the previous office action.

5. Claims 60-68 and 70-79 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments

It is noted that the rejections under 35 USC 101 and 112/first paragraph are withdrawn with regard to sequences consisting of the sequence of any one of SEQ ID NOS 1-5, however, the claims stand rejected because of additional embodiments in claims which are still rejected. The rejections with regard to sequences consisting of the sequence of any one of SEQ ID NOS 1-5 are withdrawn as the specification has set forth, in Table 1, that overexpression of a sequence of SEQ ID NO 1 could be used to differentiate between normal breast and two specific malignant breast samples, although the specification has not established that these sequences could be used in a general method of detecting breast disease or breast cancer (for the reasons already made of record in previous office actions). Table 1 of the specification shows an RNAse protection assay

using SEQ ID NO 1 where 10 times or more overexpression for two specific malignant breast samples was observed over that of any normal breast sample. Therefore, these two specific malignant breast samples could be differentiated from normal breast samples using the sequence of SEQ ID NO 1, SEQ ID NO 4, and SEQ ID NO 5 (which contain SEQ ID NO 1, sequences of SEQ ID NO 2 and 3 could be used to detect SEQ ID NO 4 and SEQ ID NO 5). The utility of the sequences is therefore dependent on their specific nucleotide composition. Degenerate coding sequences of any of these sequences, however, would not necessarily hybridize to SEQ ID NO 1-5, or would provide nonspecific hybridization such that the two malignant breast samples would not be differentiated from normal breast samples or any other tissue sample. Further, sequences "comprising" such (for example claims 63-65), could contain additional sequences on either side of SEQ ID NOS 1-4, such that the claimed nucleic acids would no longer provide selective hybridization to sequences consisting of SEQ ID NOS 1-4.

Applicants traversal of the previous rejection under 35 USC 101 was fully considered, however the arguments were not found persuasive. Applicants assert that they are puzzled by the examiner's reasoning for not finding the declaration submitted under 37 CFR 1.132, sufficient to overcome the rejections under 35 USC 101 and 112/first paragraph. Applicants state that it is well known that breast cancers spread through the lymph nodes. This argument has been thoroughly reviewed but was not found persuasive as the specification has not set forth a predictable correlation that sequences of BS106 can be used to diagnose breast cancer (although the specification has taught in table 1, that SEQ ID NO 1 could be used to differentiate between a

specific malignant breast cancer sample and normal breast sample, this is not the same as saying that BS106 nucleic acids could be used generally to detect any breast cancer sample, any diseased breast sample or be used in a diagnostic method for breast cancer, see previous office action, page 3). Applicant's response asserts that the specification teaches that BS106 can be used for a number of different purposes and cites page 5, line 2 - page 6, line 21 and page 18. This argument has been thoroughly reviewed but was not found persuasive as the sections cited by applicant teach detecting BS106 generally in a sample and do not specifically assert a utility for BS106 in detection of metastasized breast cancer to lymph node by detection of BS106 nucleic acids in lymph node. Therefore, for these reasons and the reasons made of record above and in previous office actions, the rejections of the instantly pending claims under 35 USC 101 and 35 USC 112/first paragraph, are maintained.

New Grounds of Objection and Rejection

Claim Objections

6. Claim 66 is objected to because of the following informalities: the claim is dependent on claim 59 which has been canceled. Appropriate correction is required. It is noted that this objection can be overcome by making the claim dependent on claim 79. Applicants should further note, however, that simply amending the claim to be dependent on claim 79 would raise new issues under 35 USC 112/2nd paragraph. For example, terms within claim 59, such as "said

sample", would lack sufficient antecedent basis. Such amendment (making the claim dependent on claim 59) would also raise new issues under 35 USC 103 (see section 11, below).

Claim Rejections - 35 USC § 112

7. Claims 72-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 75 is indefinite in the recitation in step c of "contacting the first stage reaction product with at least one third oligonucleotide... with the proviso that the third oligonucleotide is located 3' to the first and second oligonucleotides utilized in step b..." and in step d of "wherein the oligonucleotides utilized in steps (b) and © are selected from the group consisting of SEQ ID NOS 1-4 and 5 or degenerate codon equivalents thereof" as the sequences of SEQ ID NOS 1-5 are sequences that overlap each other such that if two different sequences are used as the first and 2nd oligonucleotides as sense and antisense primers, ie SEQ ID NOS 1 and 3, neither SEQ ID NOS 2, 4 or 5 would be located 3'. It is further unclear if the word "primer" in this claim and in claim 72 is directed to the actual sequence of one of SEQ ID NOS 1-5 (the shortest of which is 197 nucleotides long) or to a primer that would amplify one of such sequences since primers tend to be short oligomers on the order of 20-30 nucleotides long.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (f) he did not himself invent the subject matter sought to be patented.

9. Claims 60-62, and 65 are rejected under 35 U.S.C. 102(a) as being anticipated by Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10).

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-3, (1662885, 893988, and 1209814) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. It is noted that the nucleotide sequence is an inherent property of the nucleic acid clones. Therefore, polynucleotides consisting of SEQ ID NOS 1 and 3, as well as those that could be produced by either recombinant techniques or synthetic techniques, as well as compositions of matter comprising a polynucleotide of SEQ ID NO 1 or SEQ ID NO 3 were known and used in the art at the time of filing of the instant application.

10. Claims 60-62 and 65 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention.

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-3, (1662885, 893988, and 1209814) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. It is noted that the nucleotide sequence is an inherent property of the nucleic acid clones.

11. Claims 60-62, and 65 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-3, (1662885, 893988, and 1209814) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. It is noted that the nucleotide sequence is an inherent property of the nucleic acid clones.

12. Claim 67 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession number R75793 (June 6, 1995).

Accession number R75793 teaches a nucleic acid sequence which encodes a fragment of SEQ ID NO 16 (sequence alignment provided). Nucleic acid positions 65-298 of R75793 encode amino acids 9-86 (ie: a fragment of) of SEQ ID NO 16.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claim 79 is rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10), in view of Ahern, Holly (The Scientist, vol. 9, 1995, from the Internet, pages 1-5).

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-3, (1662885, 893988, and 1209814) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. Although the nucleic acid clones are not taught in kit format, Ahern teaches that offering reagents in kit format offers scientists the opportunity to better manage their time and further teaches that buying premade reagents and kits offers scientists a convenience and the ability to save time (see p. 4, first and

2nd para). Therefore, it would have been prima facie obvious to one of ordinary skill the art at the time the invention was made to package the clones in a container for the obvious improvement of making the clones available in a convenient format to researchers.

15. Claims 63-64, 70, 72, 74, 75, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10), in view of Londos et al (US Patent 5,585,.

Claims 63-64 are drawn to expression systems and cells transfected with such, comprising the nucleic acids of SEQ ID NOS 1-3. As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-3, (1662885, 893988, and 1209814) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. Although the nucleic acid clones are not specifically taught as procured in a recombinant expression system or cell comprising such, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to construct an expression system comprising one of nucleic acids of SEQ ID NOS 1-3 to express any proteins encoded by such. Such methods were known in the art at the time of the invention as exemplified by the teachings of Londos, which teaches how transfect a cell with nucleic acids for the purposes of expression protein (col. 14, lines 53-col. 15).

Londos further teaches that the DNA can be directly detected using Southern hybridization with probes that hybridize and detect the DNA (see col. 21, lines 45-50) (claim 50).

Londos also teaches that sandwich hybridization can be used to detect the DNA where in the assay utilizes a "capture" nucleic acid covalently immobilized to a solid support and a labeled 'signal" nucleic acid in solution which bind to the target DNA (see col. 22, lines 10-30). Londos also teaches using RT-PCR for amplification of RNA sequences (see col. 29, lines 1-2). While Londos does not teach detection of mRNA using RT-PCR and subsequent hybridization and detection with a probe, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made that mRNA could be detected using RT-PCR to produce cDNA and that the cDNA could be detected with a probe specific for the cDNA sequence. Such amplification and detection methods were readily known and practiced at the time of the invention. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the detection methods taught by Londos to detect the sequences of the instantly claimed invention as Londos teaches that such methods can be used to detect nucleic acids in a test sample.

16. Claims 71, 73, 76, and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10) in view of Londos et al, as applied to claims 70, 72, 74, 75, and 77 above, and further in view of Panadian et al (US Patent 6,306,657; filed Sep. 25, 1996).

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-3, (1662885, 893988, and 1209814) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed.

Londos teaches that the DNA can be directly detected using Southern hybridization with probes that hybridize and detect the DNA (see col. 21, lines 45-50) (claim 50). Londos also teaches that sandwich hybridization can be used to detect the DNA where in the assay utilizes a "capture" nucleic acid covalently immobilized to a solid support and a labeled 'signal" nucleic acid in solution which bind to the target DNA (see col. 22, lines 10-30). Londos also teaches using RT-PCR for amplification of RNA sequences (see col. 29, lines 1-2). While Londos does not teach detection of mRNA using RT-PCR and subsequent hybridization and detection with a probe, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made that mRNA could be detected using RT-PCR to produce cDNA and that the cDNA could be detected with a probe specific for the cDNA sequence. Such amplification and detection methods were readily known and practiced at the time of the invention.

Although Londos does not teach first attaching the DNA to a solid phase before detection or attaching the probe to a solid support before contacting the DNA to the probe, Panadian teaches that some nucleic acid hybridization assays involve immobilization of the target sequence on a solid support followed by washing the remainder of the reaction mixture (see col. 3, lines 16-24). Panadian teaches that this involves techniques that attempt to either immobilize the target sequence before adding a label probe or using an immobilized labeled probe to capture the

target nucleotide sequence. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to that the methods taught by Panadian have been suitable hybridization techniques and could have been used in the methods taught by Londos for the purpose of detecting the sequences of the instantly claimed invention in a test sample.

Conclusion

17. No claims are allowable.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
1/15/03